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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/693,999	10/28/2003	Ilia Davydov	2528-10	4116

23117 7590 11/16/2004

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EXAMINER

DESAI, ANAND U

ART UNIT	PAPER NUMBER
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1653

DATE MAILED: 11/16/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

<b>Office Action Summary</b>	<b>Application No.</b>	<b>Applicant(s)</b>	
	10/693,999	DAVYDOV ET AL.	
	<b>Examiner</b>	<b>Art Unit</b>	
	Anand U Desai, Ph.D.	1653	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 20 September 2004.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 3-8,10,12,15-17,25,35-53 and 55 is/are pending in the application.
- 4a) Of the above claim(s) 5-8,10,12,15,16,25,35-53 and 55 is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 3,4 and 17 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☒ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)                        | 4) <input type="checkbox"/> Interview Summary (PTO-413)                     |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948)               | Paper No(s)/Mail Date. _____  |
| 3) <input checked="" type="checkbox"/> Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) | 5) <input type="checkbox"/> Notice of Informal Patent Application (PTO-152) |
| Paper No(s)/Mail Date <u>12/17/2003</u> .  | 6) <input type="checkbox"/> Other: _____                                    |

**DETAILED ACTION*****Election/Restrictions***

1. Applicant's election with traverse of Group I, drawn to claims 3-4, and 17 in the reply filed on September 20, 2004 is acknowledged. The traversal is on the ground(s) that it is not an undue burden to search Groups I and II, and that Groups III, and XI should be rejoined with Group I, because the chemical compounds are related. This is not found persuasive because as stated in the restriction requirement, the inventions of groups I and II are distinct and have acquired a separate status in the art, therefore restriction for examination purposes as indicated is proper. Further, the inventions of groups I, III, and XI are distinct because the composition of each group is different in structure and function. The structure of the composition in group I is drawn to a complex comprising at least one ubiquitin or a derivative thereof, and a protein, selected from a Markush group. The structure of the composition of group III is drawn to an isolated activated fragment of a protein having an exposed N-degron. The structure of the composition of group XI is drawn to a library of N-end rule ubiquitylation substrates including at least two proteins, or fragments or derivatives thereof, selected from a Markush group. Therefore, each composition would require a separate search.

The requirement is still deemed proper and is therefore made FINAL.

2. Acknowledgement is made of Applicant's request to rejoin process claims under *In re Ochiai* and *In re Brouwer* upon indication that a product claim is allowable.
3. Claims 5-8, 10, 12, 15, 16, 25, 35-53, and 55 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected inventions, there being no allowable generic or linking claim. Applicant timely traversed the

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restriction (election) requirement in the reply filed on September 20, 2004. This application contains claims 5-8, 10, 12, 15, 16, 25, 35-53, and 55 drawn to an invention nonelected with traverse filed on September 20, 2004. A complete reply to the final rejection must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01. Claims 3, 4, and 17 are currently pending and are under examination.

***Priority***

4. Acknowledgment is made of applicant's claim for priority under 35 U.S.C. 119(e). The priority date is October 30, 2002.

***Information Disclosure Statement***

5. The information disclosure statement (IDS) submitted on December 17, 2003 is being considered by the examiner.

***Specification***

6. The disclosure is objected to because of the following informalities:
7. There is a typographical error on page 5, line 7, the word, "ubiquitylation" appears to be intended to be, "ubiquitylation."
8. The use of the word, "etc" on page 43, line 8 does not convey a clear complete sentence. Suggest removing the word, "etc", or completing the sentence.

Appropriate correction is required.

***Claim Rejections - 35 USC § 112***

9. The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

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10. Claim 17 is rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

11. The phrase “assay composition” is indefinite. How is the “assay composition” distinguished from a composition?

12. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

13. Claims 3, 4, and 17 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Claims 3, 4, and 17 are drawn to a complex or assay composition comprising a derivative of ubiquitin, and a fragment or derivative of a protein selected from the group consisting of aprataxin, tau, SLP, HMG17, PinX1, CIR, Cullin 3, HMGN3, HSPC144, and CDC6. The specification does not clearly describe the derivatives of ubiquitin, or the fragments or derivatives of a protein selected from the group consisting of aprataxin, tau, SLP, HMG17, PinX1, CIR, Cullin 3, HMGN3, HSPC144, and CDC6 that would encompass the isolated complex or assay composition. Based on the description on page 43, lines 15, and 16, a fragment can be any dipeptide.

***Claim Rejections - 35 USC § 102***

14. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

15. Claims 3, 4, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Maeda, I. et al. (FEBS Letters 494: 181-185 (2001)). Maeda, I. et al. disclose an isolated complex comprising at least one ubiquitin and a protein, wherein the protein is Cullin 3. 293T cells were co-transformed with myc-tagged Cullin 3, and a small RING finger protein, ROC1 (subunit member of E3-Ubiquitin ligase). ROC1-cullin 3 immunoprecipitated protein were immobilized on protein A-agarose beads and added to an *in vitro* ubiquitination assay in the presence of ubiquitin conjugating enzymes, E1, E2, and unlabeled bovine ubiquitin. The complex was immobilized and labeled with a mouse monoclonal c-myc antibody. Figure 4 shows the ubiquitination of Cullin 3 (see pp. 184, Figure 4, lane 4, middle panel, current application, claims 3, 4, and 17).

16. Claims 3, 4, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Elsasser, S. et al. (Molecular Biology of the Cell 10: 3263-3277 (1999)). Elsasser, S. et al. disclose an isolated complex comprising at least one ubiquitin and a protein, wherein the protein is CDC6. In vitro translated CDC6 substrate was mixed in a ubiquitination assay comprising ubiquitin enzymes (including CDC43), bovine ubiquitin, and ATP. The CDC6-ubiquitin complex was immobilized on a nitrocellulose membrane and labeled with an anti-Myc antibody. The immunoblotted composition identified CDC6 protein

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that was ubiquitinated (see pp. 3270, figure 4, lane 8, current application, claims 3, 4, and 17).

17. Claims 3, 4, and 17 are rejected under 35 U.S.C. 102(b) as being anticipated by Morishima-Kawashima, M. et al. (Neuron 10(6): 1151-1160 (1993)). Morishima-Kawashima, M. et al. disclose an isolated complex comprising at least one ubiquitin and a protein, wherein the protein is tau. Morishima-Kawashima, M. et al. purified a Sarkosyl-insoluble fraction of proteins from Alzheimer's disease (AD) brain tissue. The purified fractions were run on a SDS-PAGE and immunoblotted. The tau-ubiquitin complex was immobilized on an immunoblot, and the composition was labeled with an antibody. The antibody identified ubiquitinated tau protein (see last sentence of Abstract, Figure 1, Panels A-D, Experimental Procedures section titled Purification of the PHF Smear, and Antibodies and Immunoblotting, and First sentence of Discussion, current application, claims 3, 4, and 17).

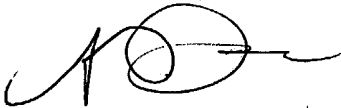
Any inquiry concerning this communication or earlier communications from the examiner should be directed to Anand U Desai, Ph.D. whose telephone number is (571) 272-0947. The examiner can normally be reached on Monday - Friday 9:00 a.m. - 5:30 p.m..

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jon P. Weber can be reached on (517) 272-0925. The fax phone number for the organization where this application or proceeding is assigned is 703-872-9306.

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Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

November 5, 2004

A handwritten signature in black ink, consisting of a large, stylized 'K' followed by a horizontal line.A handwritten signature in black ink that reads "Karen Cochrane Carlson PhD".

KAREN COCHRANE CARLSON, PH.D  
PRIMARY EXAMINER